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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/693,308	10/24/2003	Frank Grosveld	CARP0015-100	1498
34132	7590	05/08/2009	EXAMINER	
COZEN O'CONNOR, P.C.			SINGH, ANOOP KUMAR	
1900 MARKET STREET				
PHILADELPHIA, PA 19103-3508			ART UNIT	PAPER NUMBER
			1632	
			MAIL DATE	DELIVERY MODE
			05/08/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)
	10/693,308	GROSVELD, FRANK
	Examiner	Art Unit
	ANOOP SINGH	1632

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 07 April 2009 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) The period for reply expires 3 months from the mailing date of the final rejection.
- b) The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because

- (a) They raise new issues that would require further consideration and/or search (see NOTE below);
- (b) They raise the issue of new matter (see NOTE below);
- (c) They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).

5. Applicant's reply has overcome the following rejection(s): _____.

6. Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7. For purposes of appeal, the proposed amendment(s): a) will not be entered, or b) will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: 2, 4, 7-8, 10-11, 33-36, 39, 41-42.

Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).

9. The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).

10. The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. The request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See Continuation Sheet.

12. Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____

13. Other: _____.

/Valarie Bertoglio/
Primary Examiner, Art Unit 1632

Continuation of 11. does NOT place the application in condition for allowance because: The amendments to claims 2 and 41 and arguments are not persuasive to overcome outstanding rejections of the record, because the claim amendments are not in compliance and therefore these amendments have not been entered.

The Examiner maintains the rejection of claims 2, 4, 7-8, 10-11, 33-36, 39, 41-42 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for the reasons of record. Applicants arguments based on the proposed amendments are not persuasive, because the claim amendments have not been entered, as proposed claims 2 and 41 show deletion of more than five consecutive characters by using double brackets. The rejection of claims 2, 4, 7-8, 10-11, 33-36, 39, 41-42 are maintained for the reasons of record as applicant's arguments all rely on the not entered claim amendments.

Claims 2, 4, 7-8, 10-11, 33-36, 39, 41-42 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement for the reasons of record. Applicants' arguments and proposed amendments to the claims filed April 7, 2009 have been fully considered but are not persuasive because the claim amendments have not been entered for the reasons discussed above. To the extent arguments apply to the pending claims, Applicant arguments filed on 4/7/2009 have been fully considered but they are not fully persuasive. Applicants' arguments based on the proposed amendments that VHH locus is integrated in the genome (see page 9 of the argument) and naturally occurring VHH coding sequence are not persuasive because the proposed claim amendments have not been entered. It is emphasized that pending claims broadly read on VHH locus that is episomally maintained in a non human mammal. The specification has not provided working examples correlating to generating a single heavy chain antibody in response to any antigen in a mouse having claimed locus that is episomally maintained that generates heavy chain antibody. As stated before the single heavy chain antibody require involvement of VHH germline gene in which the interface residues are modified and the availability of the HCAB-specific CH (Cg) gene. It is emphasized that neither specification nor prior art provide any details of transcript processing and the extent of the CH1 removal from the VHHDJ-Cg primary transcript. Applicants have extensively relied on a post filing art of Janessens et al (Proc. National Academy of Science, 2006, 15130-15130, art of record) for enabling support that uses specific elements in the VHH locus (germ-line VHHs) that were chosen with hydrophilic amino acid codons at positions 42, 50, and 52, one with and one without a hydrophilic amino acid at 49 that is identical to IGHV1S1. The specification fails to provide structure of transgenic loci that require specific modification set forth in VHH1 or VHH2 as disclosed in Janssens in germline configuration capable of undergoing class switching to generate a single heavy chain antibody. Therefore, rejections pertaining to these issues are maintained for the reasons of record. Applicants' arguments with respect to specific modification capable of class switching is persuasive, therefore rejection pertaining to this issue is withdrawn.

Anoop Singh
AU 1632